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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/927,122	08/10/2001	Daniel P. Gold	30795-702.201	4261

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EXAMINER	
SCHWADRON, RONALD B	
ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/927,122	GOLD ET AL.	
	Examiner	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1,3,8-15,18-38 is/are pending in the application.

4a) Of the above claim(s) 18,19,22 and 38 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1,3,8-15,20,21,23-37 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. Applicant's election with traverse of the species (a) in the reply filed on 5/24/07 is acknowledged. The traversal is on the ground(s) that are stated. This is not found persuasive because of the following reasons. Regarding applicants comments, the species (a) and (b) referred to in the Office Action of 4/4/07 are chemically and functionally distinct and have different amino acid sequences. Regarding applicants comments, the species of (a) was not present in the claims until after the Office Action of 7/7/06 and therefore has never been searched.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1,3,8-15,20,21,23-37 are under consideration.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1,3,8-15,20,21,23-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no support in the specification as originally filed for the recitation of "Cbeta or Calpha region is thirty amino acids or less" in claim 1. Regarding applicants comments, the cited passage of page 12 of the specification indicates that:
"In other preferred embodiments, the chimeric proteins may comprise at least a portion of a Vbeta or Valpha chain of a TCR, plus a portion of **that TCR chain's constant region** of about thirty amino acid residues or less, and at least a portion of an immunoglobulin constant region.".
Thus, said teaching is limited to the use of constant region from the original TCR from which the Vbeta or Valpha was derived. The claims under consideration encompass use of a Cbeta or Calpha region that is thirty amino acids or less and derived from any

TCR. Regarding the cited passages of the specification, page 13-14, said passages also appear to refer to the constant region that is naturally associated with a specific TCR V region. In addition, said passage is restricted to use of IgGgamma1 Ig heavy chain and kappa light chain and refers to use of the entire Vbeta region..

There is no written description of the scope of the claimed inventions in the specification as originally filed (aka the claimed invention constitute new matter).

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. The rejection of claims 1,2,4-17,23-27,29-31,33-36 under 35 U.S.C. 102(b) as being anticipated by Weidanz et al. (WO 99/18129) as per the previous Office Action is withdrawn in view of the amended claims and cancellation of claims that have been cancelled.

7. The rejection of claims 1,2,4-8,10-13,15-17,23-27,31,33-36 under 35 U.S.C. 102(b) as being anticipated by McKeever et al. as per the previous Office Action is withdrawn in view of the amended claims and cancellation of claims that have been cancelled.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The rejection of claims 1,2,4-17,23-27,29-31,33-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weidanz et al. (WO 99/18129) in view of Brostoff et al. (WO 94/25063) as per the previous Office Action is withdrawn in view of the amended claims and cancellation of claims that have been cancelled.

10. Claims 1,3,8-15,23-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weidanz et al. (WO 99/18129) in view of Lebowitz et al.

Weidanz et al. disclose a TCR Vbeta/Cbeta attached by a linker to a Valpha/Calpha wherein said construct is linked to human Ig C kappa constant regions (see claims 1-22 and page 17). Weidanz et al. disclose use of Calpha fragment or Cbeta fragment in said construct (see claims 4 and 5). Weidanz et al. teach that the Calpha can be up to 22 amino acids (see page 15, lines 26-28). Weidanz et al. disclose use of Cbeta fragments in said construct (see claim 4) wherein the optimal length would be determined by routine experimentation. Weidanz et al. disclose an in vivo method of treatment with said construct to treat disease mediated by pathogenic T cells (see claim 39, page 11). The TCR chains used in the chimeric protein are derived from pathogenic T cells in the patient (see page 11 and 22-26). Weidanz et al. disclose that the chimeric protein can be made in insect cells using baculovirus. The recitation of a particular means wherein the baculovirus produced chimeric protein is made carries no patentable weight. Weidanz et al. teach polyvalent multimers of the aforementioned chimeric TCR wherein said molecules would have multiple constant region chains (see page 35, last paragraph). Weidanz et al. do not teach said method using the chimeric protein of claim 1 containing a Ig heavy chain constant region. Lebowitz et al. teach soluble high affinity chimeric TCR proteins that contain a TCR alpha and beta chains (Valpha plus Calpha and Vbeta plus Cbeta) attached to IgGamma1 heavy and kappa light chains (see Figure 1 and 2). A routineer would have prepared the protein using human constant region fragments for use in humans as per disclosed by Weidanz et al. using Ig heavy and light chains of Lebowitz et al. One of ordinary skill in the art would have been motivated to do so because Lebowitz et al. disclose that the advantages of using IgG scaffold (aka both heavy and light chain constant regions) in said chimeric constructs (se page 179, first column, first complete paragraph). It would have been

prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Weidanz et al. disclose an in vivo method of treatment with chimeric T cell receptors to treat disease mediated by pathogenic T cells which express said receptor and the construct used, except for a Ig heavy chain constant region whilst Lebowitz et al. teach soluble high affinity chimeric TCR proteins that contain a TCR alpha and beta chains attached to Ig heavy and light chains. One of ordinary skill in the art would have been motivated to do the aformentioned because Lebowitz et al. teach the advantages of using IgG scaffold (aka both heavy and light chain constant regions) in said chimeric constructs.

Regarding applicants comments, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Weidanz et al. disclose an in vivo method of treatment with chimeric T cell receptors to treat disease mediated by pathogenic T cells which express said receptor and the construct used, except for a Ig heavy chain constant region whilst Lebowitz et al. teach soluble high affinity chimeric TCR proteins that contain a TCR alpha and beta chains attached to Ig heavy and light chains. One of ordinary skill in the art would have been motivated to do the aformentioned because Lebowitz et al. teach the advantages of using IgG scaffold (aka both heavy and light chain constant regions) in said chimeric constructs.

11. Claim 37 is rejected under 35 U.S.C. 103(a) as being unpatentable over as Weidanz et al. in view of Lebowitz et al. applied to claims 1,3,8-15,23-36 above, and further in view of Brostoff et al. (WO 94/25063).

The previous rejection renders obvious the claimed method except wherein it can be used to treat T cell lymphoma. Brostoff et al. teach treatment of T cell lymphoma by administration of TCR derived from a T cell lymphoma (see page 2, last paragraph, continued on next page and page 3, last paragraph, continued on next page). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Weidanz et al. disclose an in vivo method of treatment with chimeric T cell receptors to treat disease mediated by pathogenic T cells which express said receptor and Brostoff et al. teach treatment of T cell lymphoma (a T cell mediate pathology) by administration of TCR derived from a T

cell lymphoma (see page 2, last paragraph, continued on next page and page 3, last paragraph, continued on next page). One of ordinary skill in the art would have been motivated to do the aformentioned because Brostoff et al. teach treatment of T cell lymphoma (a T cell mediate pathology) by administration of TCR derived from a T cell lymphoma.

12. Claims 20,21 are rejected under 35 U.S.C. 103(a) as being unpatentable over as Weidanz et al. in view of Lebowitz et al. applied to claims 1,3,8-15,23-36 above, and further in view of Bonnem et al. (WO 94/01133).

The previous rejection renders obvious the claimed method except wherein said method can be used with GM-CSF. Bonnem et al. disclose that GM-CSF can be administered to increase the immune response to an administered antigen (see claim 1 and abstract). Weidanz et al. disclose that their method can act by immunizing humans against pathogenic T cells which express the target TCR (see page 6, last paragraph). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Weidanz et al. disclose that their method can act by immunizing humans against pathogenic T cells which express the target TCR whilst Bonnem et al. disclose that GM-CSF can be administered to increase the immune response to an administered antigen. On of ordinary skill in the art would have been motivated to do the aformentioned because Bonnem et al. disclose that GM-CSF can be administered to increase the immune response to an administered antigen.

13. No claim is allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is 571 272-0851. The examiner can normally be reached on Monday-Thursday 7:30-6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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